NAVAL HEALTH RESEARCH CENTER

REPRODUCTIVE OUTCOMES AMONG GULF WAR ERA U.S. MILITARY VETERANS: MISCARRIAGES MAY BE INCREASED

P. A. Sato
K. M. Hiliopoulos
L. Wang
C. M. Anderson
D. R. Kamens
J. M. Major
C. B. Morn
P. P. Poblete
A. C. Zau
G. C. Gray

20040121 038

Report No. 00-42

Approved for public release; distribution unlimited.

NAVAL HEALTH RESEARCH CENTER P. O. BOX 85122 SAN DIEGO, CA 92186-5122



BUREAU OF MEDICINE AND SURGERY (MED-02) 2300 E ST. NW WASHINGTON , DC 20372-5300



Reproductive Outcomes among Gulf War Era US Military Veterans:

Miscarriages May be Increased

Paul A. Sato, M.D., MPH¹
Katia M. Hiliopoulos, MPH, MBA^{1,2}
Linda Wang, BS¹
Christy M. Anderson, BS^{1,3}
Deborah R. Kamens, MBA¹
Jacqueline M. Major, MS^{1,3}
Cassandra B. Morn, BA¹
Pamela P. Poblete, MPH^{1,4}
Andrew C. Zau, MPH¹
Gregory C. Gray, M.D.¹

¹DOD Center for Deployment Health Research Naval Health Research Center P. O/ Box 85122 San Diego, California 92186-5122

²Agouron Pharmaceuticals, Inc., San Diego

³Tobacco Control Policies Project University of California, San Diego

⁴Center for Behavioral and Community Health Studies San Diego State university

14 November 2000

Report No. 00-42, supported by the Office of the Assistant Secretary of Defense, Health Affairs under research work unit DOD (HA) Reimbursable, Deployment Health Research Studies-60002. The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the U.S. Government. Approved for public release; distribution unlimited. This research has been conducted in compliance with all applicable Federal Regulations governing the protection of human subjects in research.

ABSTRACT (247 words)

Context Veterans of the 1991 Gulf War may have had exposures adversely affecting their reproductive health. We examined the reproductive health of male Gulf War veterans and their spouses in a nationally representative sample of 1991-era US military personnel.

Objective Compare the reproductive health in a nationally representative sample of 1991-era male US military veterans and their spouses, Gulf War deployed and nondeployed.

Design Self-completed postal survey of 1991-95 outcomes in a probability-based sample of male 1991-era veterans.

Setting Male US military veterans, married and aged 18-33 years in 1991, and their spouses.

Study Participants A total of 8915 Gulf War deployed and nondeployed subjects were selected after stratifying for branch of service and component.

Main Outcome Measures Self-reported reproductive outcomes.

Results In total, 2716 Gulf War and 2169 nondeployed veterans responded, a participation rate of 62.0%, adjusting for 1032 undeliverable questionnaires. Nondeployed veterans were underrepresented in the respondents (p<0.001). No significant differences were found in the odds of reporting births, ectopic pregnancies, or stillbirths. Male Gulf War veterans reported an increased odds of their spouses experiencing a miscarriage in 1991-92 (adjusted odds ratio=1.72; 95 percent confidence interval 1.14, 2.59). This effect did not persist into 1993-95.

Conclusions Spouses of male Gulf War veterans experienced increased odds of miscarriages in 1991-92. Given the possibility of response bias due to underrepresentation of nondeployed veterans, among other reasons, additional studies will be needed to confirm the nonpersistent postwar increase in miscarriages among couples with male Gulf War veterans.

A number of veterans of the 1991 Gulf War have complained of diverse symptoms and illnesses, possibly related to their military service during that conflict. Concern has been voiced that some of these veterans may have had exposures that adversely affected their reproductive health ¹. A US General Accounting Office report ² identified the need to examine these concerns in nationally representative samples of US military service members including all services (Army, Navy, Air Force, Marine Corps) and components (active duty, reserve, and National Guard). We report here on male US military veterans from the Gulf War era, as a companion article to our report on the reproductive outcomes among female US military veterans (Sato et al, Naval Health Research Center, unpublished manuscript). Our objective was to examine the reproductive health of Gulf War-era male US military veterans, deployed and nondeployed, and their spouses in a nationally representative sample with proportionate representation of all services and components.

METHODS

Study population

Male US military veterans who were in the Gulf War theater of operations between August 1, 1990, and July 31, 1991, aged 18-33 years and married on February 1, 1991 were considered Gulf War veterans. Married male veterans aged 18-33 years of the same era but not deployed to the Gulf War theater of operations were defined as nondeployed veterans. All service and components were represented in the study population. Deployment status was determined by DMDC from hostile fire pay records, and military unit deployment data.

This study was conducted in accordance with the Protection of Human Subjects guidelines from the US Department of the Navy. The study protocol and informed consent

issues were reviewed for this purpose by our institutional review board, and approval for the study obtained.

Sample size

The minimum sample size requirement was estimated at 8000 based on detecting a 10 percent difference in rates of miscarriages between Gulf War veterans and nondeployed veterans. However, because we were dealing with a highly mobile and young population several years after the Gulf War, we selected a total of 10 000 individuals through a probability-based selection process, to make allowances for losses. Acceptable limits of β -error were defined as 0.20, and α -error at 0.05.

Of the approximately 2 500 000 male active-duty, reserve, and National Guard service members in 1991, approximately 644 000 were deployed to the Gulf War theater of operations. From this population, a stratified random sample of 5000 with proportionate allocation of service and their components was generated for each of the Gulf War veterans and nondeployed veterans groups, for the total sample of 10 000.

Questionnaire

A four-page, self-completed postal questionnaire composed of both multiple-choice and open-ended questions was developed and field-tested. To enhance the validity and generalizability of the results, previously standardized questions were used in the questionnaire wherever possible. Sources of the questions included the Chicago Reproductive Health Survey (National Institute of Environmental Health Sciences, Research Triangle Park, NC, 1991), the National Survey on Family Growth, Cycle IV (National Center for Health Statistics, Hyattsville, MD, 1988), and the National Maternal and Infant Survey (National Center for Health Statistics, Hyattsville, MD, 1988). The questionnaire obtained demographic data (race/ethnicity and

educational attainment), as well as information on military component, deployment, and information on the main outcomes measures: reproductive outcomes (livebirths, ectopic pregnancies, miscarriages/spontaneous abortions, and stillbirths).

Reproductive outcomes

For each reproductive outcome, respondents were encouraged to consult with their spouses and specify the date of the outcome, and whether the pregnancy had resulted in ectopic pregnancy (fetal death after extra uterine implantation), miscarriage (fetal death before 22 weeks of gestation), stillbirth (fetal death at or after 22 weeks of gestation), or livebirth (child born alive).

Information on birth weight, gestational age, and the sex of the infant was sought for each live birth. Subjects were asked to complete separate entries for each outcome in a multiple-birth pregnancy.

Pilot study

The survey questionnaires were pilot-tested among 14 individuals from outside the study population. Information from the pilot study was used to finalize the survey instrument.

Data collection

Survey Mailing Process. The 10 000 initially selected were mailed a preliminary notification letter. These letters, mailed in February 1996, introduced the study to prospective participants and attempted to answer all anticipated questions about the study's purpose and objectives. It also sought to address any concerns about confidentiality of information that would be collected.

Study questionnaires were mailed to the 8915 subjects whose preliminary letters were not returned as undeliverable. Three rounds of questionnaires were mailed out over the next 18 months. Each mailing targeted those individuals who had not responded within 6 months to the

preceding mailing. Specific study letterheads and logos were used for all correspondence with study subjects during the mailings to make our mailings easily distinguishable from other mail. To encourage responses, reminder postcards were sent 3 weeks after each mailing.

For subjects remaining on active duty, we routed surveys through their commanding officers. For the attention of these commanders, we attached letters from each service's Surgeon General, stressing the importance of this study and requesting that the commanding officers encourage potential study subjects to participate.

For subjects no longer on active duty, cover letters that incorporated comments describing other respondents' feelings about the significance and value of the study were included with the questionnaires, again to encourage participation.

Tracing correct addresses. Addresses obtained from the DMDC were used for initial mailings. If questionnaires were returned as undeliverable, additional sources were accessed to identify the most likely current valid addresses: the locator services of each branch of the military, Internal Revenue Service address data, and a commercial locator agency.

Collecting Missing Information. After completion of the third and final mailing, 1042 subjects were re-contacted by telephone to obtain missing information on incomplete questionnaires or to clarify responses. Five attempts to establish telephone contact were made to each apparently accurate phone number either obtained from the survey or acquired through an outside locator service. Attempts to contact by phone were made both during the week (2-3 times in the evening), as well as during weekends between 9 a.m. and 5 p.m. in the call recipients' time zone, before a subject survey was classified as "unreachable."

Supplemental information was obtained for 65.9% (687/1042) with missing information. Information could not be obtained from the remaining 355 individuals. Of these, 107 had

refused to provide further information over the telephone, or they could not be interviewed despite repeated attempts at contact through an apparently correct telephone number. Correct telephone numbers could not be identified for the other 248, despite multiple attempts.

Validation

To validate the answers provided by self-reported questionnaire, electronic hospital discharge records from US Department of Defense hospitals were compared with survey responses. Only subjects who remained on active duty during 1991-1995 were examined, since only data on hospitalizations among service members on active duty were available. Responses were considered validated if the same or similar diagnosis was noted in the records within the same calendar year. No electronic data were available for hospitalizations outside Department of Defense facilities, or for ambulatory visits for the time period of interest, 1991-1995.

Statistical Analysis

Frequencies of demographic data were generated for univariate analysis. Age was determined as of February 1, 1991. A multivariate logistic regression model was developed to generate odds ratios (OR), adjusted by age, race/ethnicity, highest level of education attained, military component, and pre-1991 reproductive outcomes. All reproductive outcomes occurring up to December 31, 1995, in the sample populations were included in the analysis. Post–Gulf War reproductive outcomes were defined as those occurring after May 31, 1991; outcomes at or before that date were defined as "pre-1991 outcomes". Univariate analysis was carried out for outcomes such as multiple births, ectopic pregnancies, and stillbirths, where sample size limitations excluded the use of multivariate models. Singleton and multiple births were analyzed separately.

RESULTS

The sample included 8915 selected subjects. Overall, 4885 (54.8 percent) of subjects returned a questionnaire; of these, 563 were returned blank. Excluding 1032 questionnaires that could not be delivered despite several attempts at tracing, the participation rate was 62.0 percent (4885/7883). Responses for singleton and multiple births were analyzed separately. Subjects who were nondeployed, reservists, Army veterans, and black were less likely to have participated in the study (Table 1).

Total births

A total of 5158 singleton livebirths, and 66 twin/higher-order multiple births were reported by Gulf War veterans and nondeployed veterans. Of these, 2376 singleton births and 21 twin births occurred after the Gulf War. The proportional distribution of these births was similar to that reported by the National Center for Health Statistics for all births in the US in 1995 (Figure 1). The odds of birth in couples with male Gulf War veterans in the four years following the conflict did not differ significantly from that among nondeployed veterans, after adjustment for the effects of influential covariates (adjusted odds ratio (OR)= 0.81, 95 percent confidence interval (CI) 0.57, 1.15) (Table 2).

Macrosomia (birth weight ≥4000 g)

Singleton macrosomic infants represented 13.4 percent (318/2376) of all births occurring after the Gulf War. A total of 655 macrosomic births were reported by subjects. No statistical association was found between Gulf War deployment and delivery of macrosomic babies post-Gulf War (adjusted OR= 0.89, 95% CI 0.69, 1.17). Previous macrosomic births was associated with an increased odds of such a birth post-Gulf War (adjusted OR= 3.94, 95 percent CI 2.35, 6.60) (Table 2).

Normal weight singleton births

Singleton babies born with normal birth weights (2500-3999 g) accounted for 81.1 percent (1926/2376) of all singleton births reported following the Gulf War. There were a total of 4202 normal weight singleton births reported by subjects. The odds of having a normal birth weight infant were no different among Gulf War veterans when compared with nondeployed veterans (adjusted OR= 1.06, 95 percent CI 0.86, 1.31). Previous normal weight singleton births was highly associated with the odds of a similar birth post-Gulf War (adjusted OR= 4.65, 95 percent CI 3.19, 6.79) (Table 2).

Low birth weight (LBW) singleton births

Respondents reported 119 births with birth weights of 1500-2500 g, or 5.01 percent (119/2376) of all reported singleton births post-Gulf War. An additional 13 (0.55 percent of births post-Gulf War) were born with birth weights of <1500 g. Overall, a total of 301 LBW (<2500 g) births were reported by subjects. Given the small number of very low birth weight (<1500 g) births reported, all LBW births (<2500 g) were analyzed together. No statistically significant association between Gulf War deployment, and fathering LBW infants post-Gulf War was identified (adjusted OR= 1.38, 95 percent CI 0.91, 2.09). Previous LBW births were associated with significant odds of a similar birth post-Gulf War (adjusted OR= 8.01, 95 percent CI 3.35, 19.12) (Table 2).

Twin and other multiple births

Respondents reported a total of 21 twin births after the Gulf War, out of a total of 66 twin births. There were no triplet or higher order births. The multiple birth ratio was 8.8/1000 livebirths. No statistical association between Gulf War deployment and twin/multiple births was detected (age adjusted OR= 0.86, 95 percent C.I. 0.47, 1.56) (data not shown).

Total reproductive losses

In the period following the Gulf War, a total of 385 reproductive losses, consisting of 25 stillbirths, 50 ectopic pregnancies, and 310 miscarriages were reported. Overall, a total of 801 reproductive losses were reported. The odds of reproductive losses overall was no different between Gulf War veterans and nondeployed veterans post-Gulf War (adjusted OR= 1.25, 95 percent CI 0.98, 1.59) (Table 3).

Stillbirths

Forty-four stillbirths were reported by subjects, of which 25 occurred post-Gulf War. No statistically significant differences in the odds for stillbirths between Gulf War veterans and nondeployed veterans was identified (adjusted OR= 1.32, 95 percent CI 0.52, 3.34) (Table 3).

Ectopic pregnancies

None of the 82 ectopic pregnancies reported overall resulted in a livebirth. Fifty ectopic pregnancies were reported in the period following the Gulf War. No statistical association between ectopic pregnancy and Gulf War deployment status was found (adjusted OR= 0.92, 95 percent CI 0.49, 1.72) (Table 3).

Miscarriages/spontaneous abortions

A total of 675 miscarriages were reported, of which 310 were post-Gulf War. After adjustment for the contributing effects of age, race/ethnicity, educational status, and military component, male Gulf War veterans were at increased odds of fathering a miscarriage postwar (adjusted OR= 1.32, 95 percent CI 1.02, 1.73). When the post-Gulf War years were analyzed in more detail, the increased odds of miscarriage were in the first 2 years following the conflict (adjusted OR= 1.72, 95 percent CI 1.14, 2.59) (Table 4).

Validation of self-reported outcomes

Table 5 presents the percentage of reported reproductive outcomes in which medical records validated questionnaire responses. Validation of reported miscarriages was low.

COMMENT AND CONCLUSIONS

Several previous studies have examined the possibility of adverse reproductive outcomes among 1991 Gulf War veterans. Penman et al. ³ found no association of Gulf War deployment with ill health or birth defects in 2 units of the Mississippi National Guard. Internal Air Force ⁴ and Army ⁵, ⁶ investigations of pregnancy outcomes and miscarriages in Gulf War veterans also found no consistent pattern.

Other studies identified potential sources of concern. A postal survey of present and former Pennsylvania and Hawaii active-duty, Reserve, and National Guard service members 7, found that deployed reservists had a greater likelihood of reporting "menstrual difficulties" than nondeployed reservists. A study among Iowa military veterans found a higher prevalence of complaints of sexual discomfort among Gulf War veterans and their female partners 8.

With regard to birth defects, to date no increased general or specific risk related to Gulf War deployment has been definitively identified to date 9, 10

Our finding of an increased odds for male Gulf War veterans reporting that their spouses had a miscarriage in the first 2 years following the Gulf War, lends some support to the hypothesis of an increase in adverse reproductive outcomes in Gulf War veterans. However, in our view this finding should be interpreted in the context of the following: (a) the absence of a similar finding among female Gulf War veterans (Sato et al, Naval Health Research Center, unpublished manuscript), despite having studied male and female veterans using similar methods; (b) the possibility of response bias, given the underrepresentation of nondeployed

veterans in the responders when compared with the sample population; (c) the possibility of recall bias between Gulf War veterans and nondeployed veterans, given the low rates of validation of miscarriages; (d) the well-known difficulty in establishing population rates for miscarriages, given the frequency of occult losses, and miscarriages occurring outside of the health care system ¹¹; and finally (e) the absence of any major differences in birth outcomes between Gulf War veterans and nondeployed veterans in either male or female veterans pointing in the same direction of decreased fetal viability.

The increase risk of miscarriages post-Gulf War is consistent with the reported Vietnam War experience ¹², and with reports of increased rates in Bahrain and Kuwait postwar ¹³, ¹⁴. Known causes of miscarriages are many, but they include chromosomal abnormalities, structural anomalies of the female reproductive system, smoking, caffeine, alcohol or medication use during pregnancy by the mother, as well as sexually transmitted diseases, pesticides, manual labor, work fatigue, and stressful life events ¹¹, ¹⁵.

These risk factors have generally been established with respect to miscarriages after exposure of women. Male-mediated risk factors resulting in miscarriages remain not fully understood ¹¹, but exposure to thiocarbamate fungicide/herbicides and carbaryl pesticides in agricultural settings ¹⁶, mercury, and anesthetic gases ¹⁷, and possibly other agents, such as hydrocarbons, chlorinated pesticides and organophosphates ¹⁷, ¹⁸, have been implicated. In the Gulf War setting, we speculate that the most plausible exposures potentially causally linked to any increase in miscarriages are not only among the pesticides and hydrocarbons, but also personal and familial stress ¹⁵ postwar and after prolonged separation, as well as other factors, including maternal factors. This hypothesis would not account for why female service members

who served in the Gulf and studied by us did not experience increased odds of miscarriages postwar (Sato et al, Naval Health Research Center, unpublished manuscript).

Another accompanying article (Araneta et al, Naval Health Research Center, unpublished manuscript), reports on a related study looking at pregnancy outcomes among female Gulf War veterans on active duty, who had pregnancy-related military hospitalizations on dates suggestive of a Gulf War exposed conception. Araneta and her coworkers also noted increased odds of miscarriage among postwar conceptions reported by subjects. Their study subjects reported increased odds of ectopic pregnancies among postwar conceptions. Important methodological differences are likely to have influenced the differences in results. Subjects of the Araneta study were all female, whereas our results concern male veterans and their spouses alone. Over one-third of the subjects in the Araneta study were unmarried. Their subject selection criteria did not include age limits. We also note that study participation rates differed between the two studies, and that military hospitalizations are thought to account for less than 60% of births to active duty military families in 1998 (William Honner, DoD Birth Defects Registry, Naval Health Research Center, Personal Communication, 1999).

Several limitations were also inherent to the design of our study. The self-reported nature of the questionnaire suggests that the study results should be interpreted cautiously. We adopted a postal survey format to ensure the collection of a demographically representative sample of the services and their components. Because of this format, data on exposures and specific reproductive risk factors were not collected. The addition of questions on exposure and risk factors would have increased considerably the length of the questionnaire, given the large number of putative exposures discussed in relation to the Gulf War in 1994-1995. Further, for

many of the exposures, serious questions could have been raised as to the viability of collecting valid data using a mailed, self-completed method ¹⁹.

Although participation was relatively high in comparison to other postal surveys in military service members 7, 20 at 62.0 percent, it is possible that nonresponse could have biased our results. It is of particular concern that a disproportionate number of Gulf War veterans responded. Multivariable analysis would have helped account for much of these differences, but the possibility that our results were due to a response bias, where (in our case) the respondents differed in their miscarriage reproductive history from those who did not respond, has not been excluded.

In conclusion, while no persistent disease process affecting the reproductive health of Gulf War veterans is suggested by our results, further studies will be needed to confirm the apparent nonpersistent increase in miscarriages in the immediate post-Gulf War period among the wives of male Gulf War veterans, as well as identifying the factors underlying any such events.

ACKNOWLEDGMENTS

The authors thank Robert J. Reed, MS (Naval Health Research Center, San Diego, CA) for assistance in data validation; and Tyler C. Smith, MS (also of the Naval Health Research Center), for advising on the data analysis. We gratefully acknowledge the crucial contributions of Rebecca L. Calderon, PhD (Environmental Protection Agency, Research Triangle Park, NC) to the design of this study. We are also grateful to the Defense Manpower Data Center, Seaside, California, for its assistance in selecting the population sample.

REFERENCES

- Presidential Advisory Committee on Gulf War Veterans' Illnesses. Final report,
 December 1996. Washington, DC: US GPO; 1996.
- 2. US General Accounting Office. Operation Desert Storm: Potential for reproductive dysfunction is not being adequately monitored. Washington, DC: US GAO; 1994.
- Penman AD, Tarver RS, Currier MM. No evidence of increase in birth defects and health problems among children born to Persian Gulf War veterans in Mississippi. *Mil Med*. 1996;161:1-6.
- Eggert R. Final report of Robins AFB, Georgia investigation. . Brooks Air Force Base,
 TX: US Department of the Air Force; 1994.
- Broadnax G. Abortion rates post-Desert Storm. Washington, DC: US Department of the Army, Office of the Surgeon General; 1992.
- 6. Rosa C. Spontaneous abortion rate and the Gulf War mobilization. *J US Army Medical Department*. 1993;September-October 1993.
- 7. Stretch RH, Bliese PD, Marlowe DH, Wright KM, Knudson KH, Hoover CH. Physical health symptomatology of Gulf War-era service personnel from the states of Pennsylvania and Hawaii. *Mil Med.* 1995;160:131-6.
- Iowa Persian Gulf War Study Group. Self-reported illness and health status among Gulf
 War veterans. A population-based study. *JAMA*. 1997;277:238-45.
- Araneta M, Moore CA, Olney RS, Edmonds LD, Karcher JA, McDonough C, et al.
 Goldenhar syndrome among infants born in military hospitals to Gulf War veterans.
 Teratology. 1997;56:244-51.

- Cowan DN, DeFraites RF, Gray GC, Goldenbaum MB, Wishik SM. The risk of birth defects among children of Persian Gulf War veterans. N Engl J Med. 1997;336:1650-6.
- Kline J, Stein, Z, Susser, M. Conception and Reproductive Loss: Probabilities. In: Kline J, Stein, Z, Susser, M, eds. Conception to birth. Epidemiology of prenatal development.
 New York, NY: Oxford University Press; 1989:43-68.
- Institute of Medicine. Reproductive effects. Veterans and Agent Orange: update 1996.
 Washington, DC: National Academy of Sciences; 1996.
- 13. Rajab K, Mohammed, AM, Mustafa, F. Incidence of spontaneous abortion in Bahrain before and after the Gulf War of 1991. *Int J of Obstet and Gynecol*. 2000;68:139-44.
- Makhseed M, el-Tomi N, Moussa MA, Musini VM. Post-war changes in the outcome of pregnancy in Maternity Hospital, Kuwait. Med Confl Surviv. 1996;12:154-67.
- Neugebauer R, ,Kline J, Stein Z, Shrout P, Warburton D, Susser M. Association of stressful life events with chromosomally normal spontaneous abortion. Am J Epidemiol. 1996;143:588-96.
- 16. Savitz D, Arbuckle T, Kaczor D, Curtis K. Male Pesticide exposure and pregnancy outcome. *Am J Epidemiol*. 1997;146:1025-36.
- 17. Savitz D. Paternal exposures and pregnancy outcome: miscarriage, stillbirth, low birth weight, preterm delivery. In: Olshan A, Mattison D, eds. *Male-mediated developmental toxicity*. New York: Plenum Press; 1994:177-84.
- Olshan A, Faustman E. Male-mediated developmental toxicity. Ann Rev Public Health.
 1993;14:159-81.
- McCauley L, Joos, SK, Spencer, PS, Lasarev, M, Shuell, T. Strategies to assess validity of self-reported exposures during the Persian Gulf War. *Environ Res.* 1999;81:195-205.

20. Araneta M, Kamens DR, Gastanaga, VM, Zau AC, Schlangen KM, Hiliopoulos KM, et al. Reproductive and perinatal outcomes among conceptions and pregnancies during the Persian Gulf War. Conference on Federally Sponsored Gulf War Veterans Illnesses Research. Arlington, VA; 1998.

FIGURE 1. Birth outcomes reported by male service members, 1991-1995, by birth weight.

Footnote: * National vital statistics on births, 1995, from the National Center for Health Statistics (NCHS), presented for comparison purposes.

TABLE 1. Demographic data

	Sample		
	Population	Responders	p value
	N = 8,915	N = 4,322	
	%	%	
Deployment status			< 0.001
Nondeployed	50.14	42.23	
Gulf War deployed	49.86	57.77	
Age group, in years			< 0.001
≤19	4.60	4.19	
20-24	35.78	31.94	
25-29	36.53	38.27	
≥30	23.85	25.60	
Race/ethnicity			< 0.001
White	71.45	76.54	
Black	19.74	15.41	
Hispanic	5.06	4.56	
Other	3.75	3.49	
Highest educational level			< 0.001
High school or less	81.75	79.63	
College	9.32	11.96	

Postgraduate	1.11	1.36	
No information	7.82	7.06	
Service			< 0.001
Army	37.54	31.78	
Navy	25.81	29.39	
Air Force	24.49	27.56	
Marine Corps	12.16	11.27	
Service Component			<0.01
Active duty	92.73	96.70	
Reserve	4.53	2.00	
National Guard	2.74	1.30	
	 		

TABLE 1. Demographic data (cont)

TABLE 2. Singleton birth outcomes, by Gulf War deployment status, military, and demographic covariates

	Масг	Macrosomic	Normal w	Normal weight births	LBW	LBW* Births	All	All births
	births (births (≥4000g)	(2500	(2500-3999g)	3	(<2500g)		
	Ż	N=318	N =	N=1,926	ä	N=132	Ä	N=2,376
	AOR†	95% CI‡	AOR	95% CI	AOR	95% CI	AOR	95% CI
Deployment status								
Nondeployed §								
Gulf War deployed	0.89	0.69, 1.17	1.06	0.86, 1.31	1.38	0.91, 2.09	0.81	0.57, 1.15
Age group, in years								
≤19 §								
20-24	1.06	0.55, 2.03	0.83	0.51, 1.36	1.31	0.50, 3.44	1.02	0.47, 2.23
25-29	1.26	0.65, 2.44	0.83	0.50, 1.36	1.27	0.48, 3.39	96.0	0.43, 2.12
>30	1.24	0.61, 2.53	0.70	0.41, 1.21	1.15	0.39, 3.39	0.61	0.26-1.43
Race/ethnicity								
White §								
Black	0.49	0.31, 0.78	0.88	0.66, 1.19	2.05	1.27, 3.33	98.0	0.53, 1.37
Hispanic	0.49	0.25, 0.95	0.93	0.61, 1.41	1.11	0.49, 2.48	0.56	0.32, 0.99
Other	0.48	0.23, 1.02	69.0	0.44, 1.09	1.25	0.52, 3.01	0.59	0.30, 1.15
Highest educational level								

High school or less §								1
College	1.04	0.76, 1.44	1.10	0.86, 1.39	96.0	0.61, 1.51	1.08	0.74, 1.59
Postgraduate	1.39	0.81, 2.36	1.53	0.95, 2.47	1.30	0.56, 2.99	3.51	1.20, 10.26
Service component								
Active duty §				·				
Reserve	0.41	0.10, 1.72	1.48	0.61, 3.59	F	F	0.93	0.28, 3.11
National Guard	0.36	0.05, 2.69	1.13	0.40, 3.26	5	Б	0.25	0.09, 0.72
Pre-1991 outcomes								
None	0.99	0.45, 1.19	3.46	0.34, 5.10	2.04	0.90, 4.63	1.15	0.61, 2.18
Macrosomic births	3.94	2.35, 6.60	1.06	0.65, 1.72	1.25	0.45, 3.48	5.39	1.25, 23.25
Normal weight births	0.73	0.45, 1.19	4.65	3.19, 6.79	1.17	0.55, 2.53	1.56	0.84, 2.89
LBW births	0.26	0.06, 6.60	1.46	0.74, 2.85	8.01	3.35, 19.12	0.70	0.27, 1.83
Stillbirths/ectopics	96.0	0.21, 4.47	1.05	0.36,3.03	2.02	0.41, 10.04	0.30	0.09, 1.00
Miscarriages	1.15	0.68, 1.93	1.06	0.69, 1.63	1.43	0.62, 3.25	09.0	0.31, 1.13

* LBW: Low birth weight; † AOR: Adjusted odds ratio; ‡ CI: Confidence interval; § Reference category; ¶ Insufficient data

TABLE 2. Singleton birth outcomes, by Gulf War deployment status, military, and demographic covariates (cont)

TABLE 3. Stillbirths, ectopic pregnancies, miscarriages, and total reproductive losses

	Sti	llbirths	Ectopic pregnancies		Total	
	,				reprodu	ctive losses
•	Ŋ	N=25	1	N=50	N	=385
	AOR*	95% CI†	AOR	95% CI	AOR	95% CI
Deployment status						· ·
Non deployed ‡						-
Gulf War deployed	1.32	0.52, 3.34	0.92	0.49, 1.72	1.25	0.98, 1.59
Age group, in years		,				
<25‡						
25-29	1.10	0.41, 2.95	1.45	0.70, 2.99	1.05	0.80, 1.37
≥30	1.00	0.25, 3.96	2.09	0.88, 4.94	1.42	1.02, 1.99
Race/Ethnicity						
White ‡						
Black	1.02	0.29, 3.57	0.86	0.35, 2.15	0.82	0.57, 1.18
Hispanic, other	0.44	0.06, 3.32	0.18	0.02, 1.33	1.01	0.70, 1.46
Highest educational						
level						
High school or less ‡						
College or higher	0.62	0.24, 1.61	0.81	0.39, 1.67	1.15	0.86, 1.52
Service component						
Active duty ‡						
Reserve	§	§ .	§	§	0.78	0.30, 2.02

National Guard	§	§	2.89	0.36, 23.05	2.56	1.00, 6.55
Pre-1991 outcomes						
None	1.64	0.29, 9.26	0.97	0.33, 2.89	0.88	0.55, 1.38
Macrosomic births	2.46	0.41, 14.66	0.30	0.04, 2.48	0.59	0.31, 1.12
Normal weight births	0.93	0.18, 4.71	0.30	0.10, 0.88	0.56	0.36, 0.87
LBW births	2.80	0.30, 26.58	1.46	0.28, 7.54	1.37	0.66, 2.85
Stillbirths/ectopics	§	§	8.84	1.69, 46.30	2.62	0.94, 7.30
Miscarriages	1.86	0.36, 9.60	3.71	1.32, 10.49	1.55	0.98, 2.47

^{*} AOR: Adjusted odds ratio; † CI: Confidence interval; ‡Reference category; § Insufficient data.

TABLE 3. Stillbirths, ectopic pregnancies, miscarriages, and total reproductive losses (cont)

TABLE 4. Miscarriages, by years post-Gulf War, military, and demographic covariates

			Mise	carriages	-	
	19	91-92	19	993-95	19	991-95
	N	=121	N	T=189	N	T=310
	AOR*	95% CI†	AOR	95% CI	AOR	95% CI
Deployment status						-
Nondeployed ‡						
Gulf War deployed	1.72	1.14, 2.59	1.21	0.88, 1.67	1.32	1.02, 1.73
Age group, in years						
≤19‡	·					
20-24	2.79	0.66, 11.76	0.95	0.46, 1.93	1.17	0.62, 2.23
25-29	2.39	0.56, 10.23	1.01	0.49, 2.08	1.17	0.61, 2.25
≥30	4.19	0.96, 18.36	1.14	0.52, 2.50	1.54	0.77, 3.07
Race/ethnicity						
White ‡						
Black	0.86	0.48, 1.52	0.74	0.45, 1.23	0.77	0.52, 1.15
Hispanic, other	1.35	0.70, 2.61	1.60	0.94, 2.74	1.44	0.91, 2.28
Highest educational						
level	•					
High school or less ‡						
College	1.44	0.89, 2.33	1.06	0.72, 1.54	1.25	0.91, 1.72
Postgraduate	1.02	0.41, 2.53	2.07	1.14, 3.75	1.81	1.07, 3.06

Service component						
Active duty ‡				•		
Reserve	1.28	0.38, 4.29	0.88	0.26, 2.91	0.92	0.35, 2.39
National Guard	0.71	0.09, 5.39	3.36	1.18, 9.53	2.44	0.92, 6.47
Pre-1991 outcomes						**
None	0.84	0.41, 1.74	1.03	0.56, 1.92	0.88	0.54, 1.45
Macrosomic births	0.64	0.24, 1.75	0.75	0.32, 1.76	0.64	0.32, 1.28-
Normal weight births	0.91	0.46, 1.80	0.52	0.28, 0.96	0.63	0.39, 1.01
LBW births	0.95	0.27, 3.38	1.64	0.65, 4.14	1.41	0.64, 3.07
Stillbirths/ectopics	1.69	0.36, 7.82	1.40	0.30, 6.50	1.73	0.54, 5.55
Miscarriages	1.35	0.68, 2.69	1.05	0.53, 2.08	1.18	0.70, 1.99

^{*} AOR: Adjusted odds ratio; † CI: Confidence interval; ‡ Reference category.

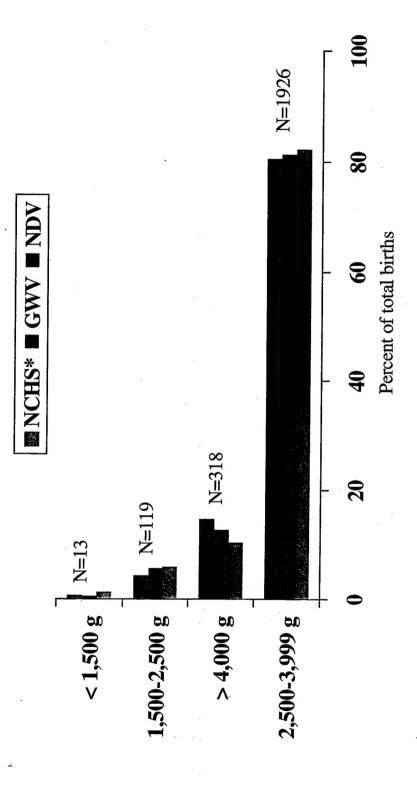
TABLE 4. Miscarriages, by years post-Gulf War, military, and demographic covariates (cont)

TABLE 5: Validation against hospitalization data of reproductive losses reported by female service members, by Gulf War deployment status

	G	ulf War veterai	ns	Nor	Nondeployed veterans			
	Reported *	Validated †	%	Reported	Validated	%		
			Validated			Validated		
Miscarriages	295	46	15.6	173	31	17.9		
Stillbirths	8	5	27.8	9	6	66.7		
Ectopic	34	9	24.5	28	7	25.0		
pregnancies								

^{*} Reproductive losses reported in study survey by subjects.

[†] Discharge diagnosis ICD-9-CM code consistent with self-reported reproductive loss recorded in database for military medical treatment facility hospitalizations for year of self-reported outcome.



REPORT DOCUMENTATION PAGE

15. SUBJECT TERMS

a. REPORT

UNCL

16. SECURITY CLASSIFICATION OF:

b.ABSTRACT

UNCL

Gulf War, male veterans, reproductive outcomes.

c. THIS PAGE

UNCL

The public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB Control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.

1. Report Date (DD MM YY) 11/14/00	2. Report Type New	3. DATES COVERED (from - to) Jan 1996 to Jul 2000
TITLE AND SUBTITLE Reproductive Outcomes am Miscarriages May Be Increa	nong Male Gulf War-era US Military Veterans: ased	5a. Contract Number: 5b. Grant Number: 5c. Program Element: 5d. Project Number:
Christy M. Anderson, B.A.; Debor Cassandra B. Morn, B.A.; Pamela M.D., M.P.H.	a M. Hiliopoulos, M.P.H., M.B.A.; Linda Wang, B.S.; rah R. Kamens, M.B.A.; Jacqueline M. Majór, M.S.; P. Poblete, B.A.; Andrew C. Zau, M.P.H.; Gregory C. Gray,	5e. Task Number: 5f. Work Unit Number: 60002 5g. CPHS Approval Number: 30276
7. PERFORMING ORGANIZATION Naval Health Research C P.O. Box 85122 San Diego, CA 92186-51	Center	9. PERFORMING ORGANIZATION REPORT
	AGENCY NAMES(S) AND ADDRESS(ES)	NUMBER Report No. 00-42
2300 E St NW	· · · · · · · · · · · · · · · · · · ·	10. Sponsor/Monitor's Acronyms(s) BUMED
Washington DC 20372-530		11. Sponsor/Monitor's Report Number(s)
12 DISTRIBUTION/AVAILABILITY Approved for public release		
13. SUPPLEMENTARY NOTES		
postwar reproductive outcomes nondeployed veterans. From 19 and married were mailed a repr the questionnaires, for a particip component, and pre-1991 repro or multiple births, ectopic pregra	words) Var have complained of ill health, with diverse symptoms is among spouses of male Gulf War veterans, compared with 996, a probability-based sample of 8,915 deployed and report to the survey. A total of 2,716 Gulf War veter in pation rate of 62.0 percent. Adjusting for age, race/ethnic ductive outcomes, no statistically significant differences mancies, or stillbirths. Male Gulf War veterans did report to the first 2 years following the Gulf War (adjusted OR= 1.7)	with those among spouses of same-era male nondeployed male military veterans aged 18-33 rans and 2,169 nondeployed veterans returned nicity, educational attainment, military s were found in the odds of reporting singleton rt increased odds that their partners had

18. NUMBER

OF PAGES

29

17. LIMITATION

OF ABSTRACT

UNCL

Standard Form 298 (Rev. 8-98) Prescribed by ANSI Std. Z39-18

19a. NAME OF RESPONSIBLE PERSON

19b. TELEPHONE NUMBER (INCLUDING AREA CODE)

Commanding Officer

COMM/DSN: (619) 553-8429